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# Is Food Intolerance a factor underlying Chronic Immune Thrombocytopenia (ITP)?

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Immune Thrombocytopenic Purpura (ITP) is an organ-specific autoimmune disorder (Karparkin, 1980) characterised by a low platelet count of less than  $100 \times 10^9/\text{l}$ .

The link between ITP and food intolerance has not been widely investigated despite anecdotal reports suggesting that food intolerance may cause ITP. It is likely that some foods produce an acute thrombocytopenia, as has been described Achterbergh et al (2012).

In general, immunoglobulin (Ig)E-mediated allergy occurs within 2 h of contact with the specific food. Food intolerance is a more general term describing an abnormal physiological response to a particular food or additive. Food intolerance is suggested when IgE allergy cannot be established yet symptoms still persist (Suen & Gordon, 2003).

IgG may contribute information about sensitivities to foods (Zeng et al, 2013) as it is produced in a delayed response to an infection and can be retained in the body for long periods due to a high synthetic rate and long half-life (Atkinson et al, 2004).

This study aimed to determine if there is a link between food intolerance and platelet count in people suffering with ITP, and whether the analysis of platelet counts plus both IgE and IgG during dietary modification can contribute to an understanding of the role of food in ITP.

A total of 50 patients of either sex aged 18–65 years suffering from chronic primary immune thrombocytopenia and a control group of 50 healthy volunteers aged 18–65 years were recruited. Further details, including exclusions, are outlined in Batty et al (2016).

Participants who were positive for IgE underwent dietary modification, where foods causing the IgE response were removed from their diet for a period of 4 weeks. A further group of ITP participants underwent dietary modification with the Elemental 028 Extra diet (E028; Nutricia, Trowbridge, UK). These participants were selected because they had the lowest platelet counts throughout the whole ITP group.

The E028, commonly used in treating Crohn disease (King et al, 1997), is a nutritionally complete liquid formula that was provided to the volunteers as 250 ml cartons.

The diet was introduced gradually over the first few days by dividing it half and half with their normal diet before commencing the elemental fully for the rest of the 4-week period. Subjects were monitored for compliance with regular phone conversations with the dietician.

Three control participants also took the elemental diet for 5–8 days.

All participants had initial blood samples taken for IgE, IgA, IgG and Tissue Transglutaminase (TTG) analysis and platelet count. ITP patients who underwent dietary modification had samples taken weekly by their GP to assess their platelet count for the duration of their dietary modification. Healthy controls who completed the E028 dietary modification had their platelets counted at the start and end of the diet. Blood samples for IgE were initially tested for 5 common allergens (FX5 Test). Positive samples were then tested for a further 43 specific foods to further identify any other responses. Samples for IgG testing were sent for analysis of 200+ food IgG sensitivities using the Genarrayt Microarray at Cambridge Nutritional Sciences (Littleport, UK).

As expected, initial platelet counts (Fig ) analysed by Mann Witney test showed a significant difference between ITP and healthy controls ( $P < 0.00001$ ; z-score-6.98).

(Insert Figure 1)

All control and ITP subjects were negative for serum IgA with TTG.

Five of the 42 ITP volunteers and three of the 30 healthy controls returned a positive total IgE result. These three controls took no further part in the study.

One of the 5 ITP volunteers with a positive total IgE was removed from the study as her platelet count was normal, and another withdrew voluntarily.

Each of the three remaining ITP subjects had IgE responses to different foods. These subjects were each instructed by the dietician as how best to remove the relevant food from their diets during the test period.

Figure indicates the mean platelet count for each group over the period of dietary intervention and shows that no significant increase in platelet count was observed. Complete removal of any foods that could cause intolerance or sensitivity (with the E028 diet) led to a slight increase in platelet count in 2 patients, followed by a subsequent decline; all of the other patients had a decline in platelet count over the course of the E028 diet.

(Insert Figure 2)

Platelet counts of the healthy controls were within normal range throughout the investigation and following dietary modification.

In the Genarrayt Microarray IgG test, a red (positive) response was above 30 arbitrary units, a yellow (borderline) response was 24–30 arbitrary units and a green (normal) response was less than 24 arbitrary units. Of the 200+ foods tested for, both ITP volunteers and healthy controls had varied responses and many controls also had a number of red and yellow responses. The results are inconclusive when trying to identify food intolerance from IgG results.

This study shows that dietary modification has no effect on platelet counts in people with chronic ITP or, indeed, healthy controls. We conclude that food intolerance is not a factor in immune thrombocytopenia. ITP patients who had positive IgE tests and underwent dietary modification did not show an improvement in symptoms or platelet counts either during or after the diet. However, there were too few subjects for meaningful statistical analysis. IgE was not analysed at the end of the modification period so it is not known whether the overall response to IgE and to those specific foods had changed.

In the initial tests for IgG, a comparison of the responses of ITP volunteers and the healthy controls showed that exactly the same foods produced the top six red responses, but in a different order. In both groups, cow's milk came up as the primary sensitivity, with a relatively similar mean arbitrary unit result ( $\pm 3\%$ ). Response of IgG antibodies to cow's milk has been previously shown to be a normal physiological response (Kletter et al, 1971).

The natural protective response of IgG suggests a response to stimulation of the immunoglobulin occurs without clinical symptoms (Mullin et al, 2010). These results suggest that when the gut is persistently exposed to certain food proteins, it responds by producing IgG but does not necessarily create a sensitivity to it. The findings in this study, however, show that that IgG tests for food intolerance are difficult to interpret.

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### **Authorship Contributions**

Paper written, analysis of samples and data conducted by Claire Batty. Patient sampling and editing of paper by John Hunter. Dietary consultation by Jenny Woolner. Haematology work up and editing of paper by Trevor Baglin. Data analysis and editing of paper by Claire Turner.

### **Disclosure of Conflicts of Interest**

No conflicts of interest noted

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### **Figure Legends**

Figure 1 – Box and Whisker plot showing initial platelet counts of ITP sufferers and healthy controls

Figure 2 – Mean platelet count over time of both IgE and elemental diet modification groups

Figure 1

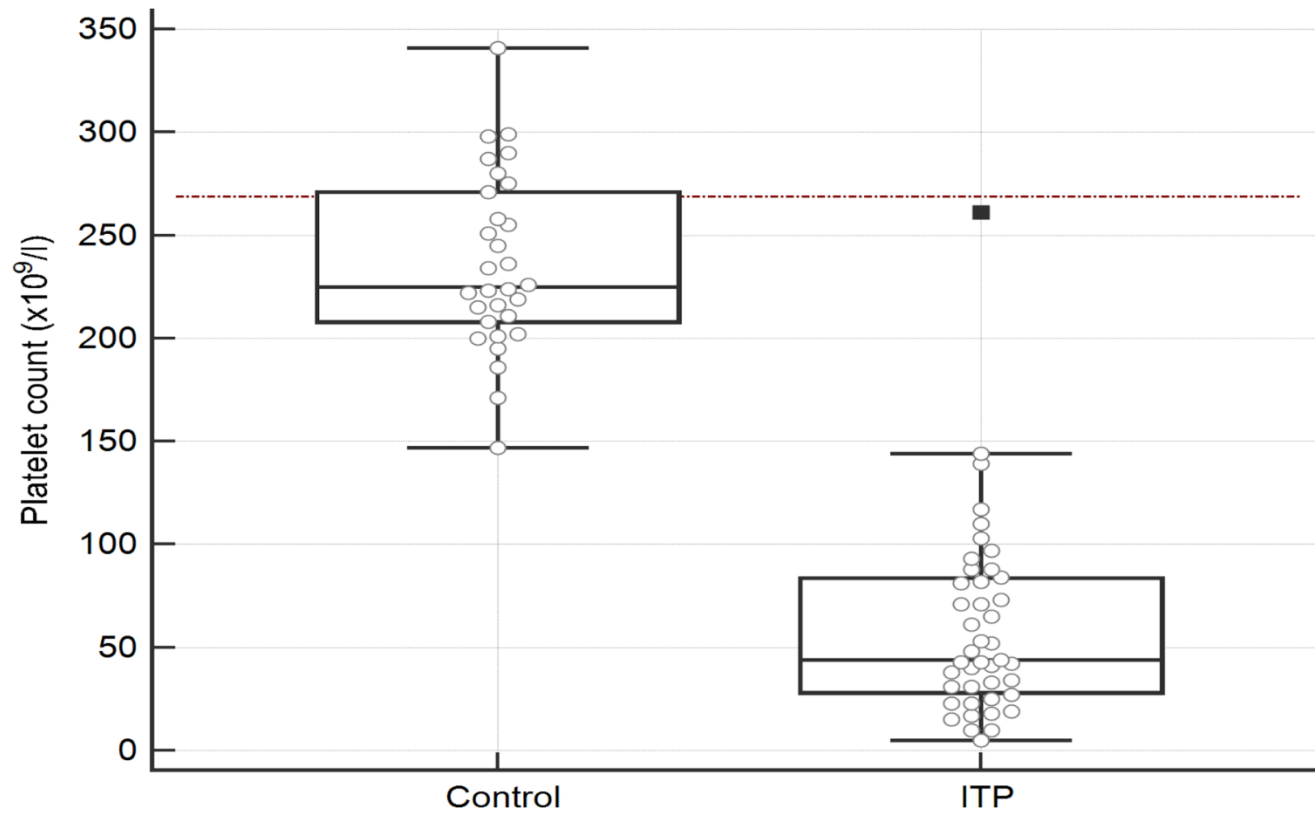


Figure 2

